REMARKS

This Amendment, filed in reply to the Office Action dated June 24, 2008, is believed to be fully responsive to each point of objection and rejection raised therein. Accordingly, favorable reconsideration on the merits is respectfully requested.

Claims 1-9, 11 and 13-20 are rejected. Claims 1-5, 7-9 and 11-20 are amended herewith solely to improve clarity. New Claim 21 is introduced. Support for recitation of "the computer model is an in silico patient that is adjusted according to the results of the … trials" in Claims 15-20 can be found throughout the specification as filed, and at, for example, the paragraph bridging pages 9 and 10. Support for recitation of "resulting in prediction of one or more trial outcomes" in Claims 18-20 can be found throughout the specification as filed, and at, for example, page 10, lines 6-7. Support for new Claim 21 can be found throughout the specification as filed, and at, for example, page 10, lines 6-7. No new matter is added by way of this amendment. Entry and consideration of this amendment are respectfully requested.

Withdrawn Rejections

Applicants thank the Examiner for withdrawal of the rejection of Claims 15-17 under 35 U.S.C. 102 (b).

Objections to the Claims

1. On page 2 of the Office Action, Claim 1 is objected to for recitation of "calculation of the dose." The Examiner asserts that such language is grammatically incorrect, and should be amended to recite "calculating the dose."

Whilst Applicants believe that one of skill in the art would readily understand what is encompassed by step (d) of Claim 1, in the interest of compacting prosecution, and without agreeing with the objection, Applicants herewith amend Claim 1 to recite "calculating the dose," in accordance with the Examiner's suggestion. Applicants submit that the amendment overcomes the objection.

2. On page 3 of the Office Action, the Examiner objects to Claim 5 for recitation of "wherein effective treatment regimen is defined." The Examiner asserts that such language is grammatically incorrect, and should be amended to recite "wherein an effective treatment regimen is defined."

Solely to advance prosecution, Applicants herewith amend Claim 5 to recite "wherein an effective treatment regimen is defined." Applicants submit that the amendment overcomes the objection.

Withdrawal of the objections is respectfully requested.

Claims 1-9, 11 and 13-20 are Definite Under 35 U.S.C. 112

On page 3 of the Office Action, Claims 1-9, 11, and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

1. The Examiner asserts that Claim 1 is indefinite in recitation of "and the phase I clinical trial is performed in parallel with performing computer simulations of the computer model" in step (b). Specifically, the Examiner contends that it is unclear as to whether the computer simulations refer to the computer model of step (a).

While Applicants submit that one of skill in the art would readily ascertain that the computer simulations of step (b) are performed on the computer model recited in step (a), in the interest of advancing prosecution, Applicants herewith amend Claim 1 to recite that the simulations are performed "using the computer model constructed in step (a)." Applicants respectfully submit that the amendment overcomes the rejection.

2. Claim 1 is further rejected as being indefinite for recitation of "wherein the at least a single dose of step (b) is incrementally increased." The Examiner contends that it is unclear as to what the single dose of step (b) refers to.

Applicants respectfully disagree, and traverse the rejection on the following grounds.

Specifically, Applicants note that step (b) of Claim 1 recites the administration of at least a single dose of the drug of step (a) to a human in a phase I clinical trial. Step (c) recites that the at least a single dose is incrementally increased in at least one dose escalation steps. Applicants respectfully submit that one of skill in the art would readily understand that the dose subject to incremental increase in step (c) is the dose administered to the human in step (b). Further, Applicants respectfully point out that dose escalation was well-known to one of skill in the art as a common feature of phase I clinical trials, as is discussed in the Eisenhauer *et al.* reference cited on page 2 of the specification as filed, the entire contents of which are incorporated therein by reference. For the foregoing reasons, Applicants submit that the bounds of the phrase "wherein the at least a single dose of step (b) is incrementally increased" would be readily ascertainable by one of skill in the art, and thus not indefinite.

3. The Examiner rejects Claim 11 as being indefinite for recitation of "wherein the decision is based on a prediction of efficacy profile of the new drug." Specifically, the Examiner contends that insufficient antecedent basis exists for recitation of "the new drug."

Solely to advance prosecution, Applicants herewith amend Claim 11 to delete recitation of "new." Applicants submit that the amendment overcomes the rejection.

4. The Examiner rejects Claims 15-20 as being indefinite for recitation of "wherein the computer model is an in silico patient that interacts with the results of the pre-clinical trials." Specifically, the Examiner asserts that it is unclear how the preclinical trials and the in silico patient is interacting.

Applicants respectfully disagree, and traverse the rejection on the following grounds.

First, Applicants respectfully point out that, as stated in the paragraph bridging pages 14 and 15 of the specification as filed, "mathematical algorithms have been developed, which simulate the key biological, pathological and pharmacological processes in a patient undergoing drug treatment." In the proceeding sentence, it is stated that "[t]his set of computerized mathematical models, in conjunction with advanced optimization algorithms have now yielded an in silico patient engine, having a range of applications designed to deliver optimal drug treatments …" (Emphasis added). Further, on page 19, 1st paragraph, it is disclosed that "[d]uring dose escalation testing in the Phase-I trials, the computer model (in silico patient) interacts with the trial, predicting the results for every step in the trial and, at termination of every step, is updated by implementing the observed effect and toxicity. In this way the computer model (in silico patient) is continuously validated and fine-tuned, to give better predictions in the next step." (Emphasis added).

From the above, Applicants respectfully submit that one of skill in the art would readily appreciate that the in silico patient is a model which comprises computerized mathematical models and advanced optimization algorithms. Applicants also submit that one of skill in the art would readily understand how the preclinical trials interact with the in silico patient, in view of the guidance provided by the specification as filed. Specifically, as noted above, the specification discloses that the experimental data obtained from the preclinical studies is used to adjust and fine-tune the in silico patient parameters. Further, in the paragraph bridging pages 16 and 17, it is stated that "[t]he model is continuously fine-tuned, by "on-line" implementation in the in silico patient, of the pre-clinical research results. Thus, the model interactively guides the empirical research to reveal the further necessary data." Thus, as discussed in the specification, an additional aspect of the interaction between the in silico patient and the preclinical studies is that further preclinical studies are designed according to the predictions of the in silico patient.

In view of the foregoing, Applicants respectfully submit that from the guidance set forth in the specification, one of skill in the art would readily understand the degree and type of interaction between the in silico patient and the preclinical studies. Nevertheless, to even further clarify the interaction between the preclinical and clinical studies and the in silico patient, Claims 15-20 are amended herewith to recite that "the computer model is an in silico patient that is adjusted according to the results of the … trials." Applicants submit that the amendments to the claims, in view of the guidance set forth in the specification, overcome the rejection.

5. On page 4 of the Office Action, the Examiner rejects Claims 18-20 as being indefinite for recitation of "wherein the prediction." The Examiner contends that insufficient antecedent basis exists for such a phrase.

Solely to advance prosecution, and without acquiescing in the rejection, Applicants herewith amend Claims 18-20 to recite that the trial, performed in parallel with a computer simulation, results "in prediction of one or more trial outcomes." Support for such an amendment can be found throughout the specification as filed, and at, for example, page 10, lines 6-7. Applicants submit that the amendments overcome the rejection.

6. On page 4 of the Office Action, the Examiner contends that Claims 18-20 are further indefinite for recitation of "wherein the at least one clinical trial is performed in parallel with computer simulation of a computer model" or "in parallel with computer simulations of a computer model." The Examiner contends that it is unclear as to how to perform computer simulations of a computer model. The Examiner suggests amending the claims to recite "performing computer simulations on a computer model" or "performing simulations using a computer model."

Solely to advance prosecution, and without agreeing with the rejection, Applicants herewith amend Claims 18-20 to recite that the simulations are performed using a computer model. Applicants respectfully submit that the amendments overcome the rejection.

Withdrawal of the indefiniteness rejections is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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